AN ANALYSIS OF CARCINOMA PENIS

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CERTIFICATE

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INTRODUCTION

"(He) that hath his privy member cut off shall not enter into the assembly of the lord" – (Deuteronomy 23:1) [130]

The prospect of losing a part or the entire penis has been a cause of considerable distress in patients with carcinoma penis[(132)]. Hanash and colleagues [(131)] have reported on 3 patients who committed suicide after penile amputation.

The incidence of carcinoma penis is only 1% of malignancies in men in developed countries like United States. But the incidence is high in developing countries like India. The stage at presentation also differs in developing countries and most of them present in late stages due to multiple factors. Though newer approaches like topical agents, Mohs micrographic surgery, laser therapy and radiotherapy may be used in early stages, surgery has remained the gold standard in carcinoma penis for many years.

"But if a cancer should infect the penis, the morbid parts are, in that case, to be immediately divided from the rest, to prevent the disorder from spreading into the adjacent sound parts, to the destruction of the patient."

-Heister's surgery, 1739.

Carcinoma penis is one of the few diseases that, when metastatic to regional lymph nodes, can be cured by regional lymphadenectomy. Involvement of the inguinal lymph nodes is the single most important prognostic factor and ilio-inguinal block dissection offers high survival rates.

The difficulty in the regional node management in carcinoma is that 50% of the clinically palpable nodes at presentation are due to infection and turn to be pathologically negative and 20% of clinically negative nodes at presentation harbor microscopic metastasis and prove positive pathologically.

However, ilioinguinal block dissection cannot be applied blindly to all patients of carcinoma penis as many of them may not warrant it and the procedure itself carries its own morbidity and complications.

Hence proper selection of patients is required to identify those who require regional lymphadenectomy in spite of clinically impalpable nodes and those who do not require regional lymphadenectomy in the node negative as well as the clinically node palpable group.

This study analyses the clinical and post surgical histopathological status of the nodes in both clinically positive and negative nodes at presentation.

This study also analyses the various epidemiological, etiological, pathological factors, clinical presentation and the management options for the primary lesion and the regional lymph nodes.

AIMS OF STUDY

1. To study and analyze the incidence, etiological factors, stage of presentation, mode of presentation, treatment policy etc., in the carcinoma penis patients at Government Royapettah hospital, Kilpauk medical college, Chennai and compare them with studies available in the literature.

2. To study the incidence of pathological involvement of inguinal nodes and compare it with clinical assessment.

REVIEW OF LITERATURE

ANATOMY OF PENIS

The penis is composed of three tubular structures, each individually encased by the tunica albuginea, a thick fibro muscular sheath. Dorsally are paired corpora cavernosa (erectile bodies) that attach to the pubic arch by crural elongations. Fibro muscular trabeculae arising from the tunica albuginea penetrate the corporal bodies, dividing them into cavernous spaces. These become engorged with blood during sexual arousal producing penile erection.

Ventrally is the corpus spongiosum through which runs the urethra. The tunica albuginea of the corpus spongiosum is thinner and more elastic than that surrounding the corpora cavernosa.

Buck's fascia, deep layer of superficial abdominal fascia, encloses the corpora cavernosa in one compartment and spongiosa in the other. This allows spongiosa to be readily dissected free of its attachments during urethrostomy.

The ischiocavernosus and bulbospongiosus muscles lie above Buck's fascia but beneath the superficial penile and colles fascia.

BLOOD SUPPLY

The penis is supplied by two arterial systems: superficial from the external pudendal arteries and deep from the internal pudendal arteries.

The superficial blood supply lies above the Buck's fascia and consists of paired superficial penile arteries that divide into dorsolateral and ventrolateral branches. Most of the blood to the penis, however, arises from the internal pudendal arteries (anterior branches of hypogastric) that bifurcate to form the perineal artery and the penile artery.

The penile artery pierces the urogenital diaphragm along the medial margin of the inferior ischial ramus and divides into three branches: the bulbourethral artery, the cavernous artery and the deep dorsal artery. The bulbourethral artery is usually short and of large caliber, pierces Buck's fascia and enters bulbospongiosum. The dorsal artery runs along the dorsum of the penis and produces 3-10 circumflex branches that course around the lateral surface of the corpora. Its terminal branch supplies the glans penis. The cavernosal artery enters the corpora cavernosa and runs the penile shaft, generating small vessels (helicine arteries) that constitute the erectile apparatus.

The penis is drained by three venous systems: superficial, intermediate and deep [(5) (6) (7).] The superficial veins located in the dartos fascia on the dorsal lateral aspects of the penis join at the penile base to form single superficial vein that, most frequently enters the left vein.

The intermediate system consists of the deep dorsal and circumflex veins, located below Buck's fascia. They originate from small veins within the erectile spaces and those emerging from the glans penis.

The deep drainage system consists of the crural and cavernosal veins, which empty into either the deep dorsal vein or the periprostatic plexus. The veins of these three systems have variable communication with each other.

LYMPHATICS

The glans penis is drained by 3 lymphatic channels, through skin, through the mucosa and one beneath the mucosa. The trunks of all three drain to the frenum where they may communicate with the lymphatics from the urethra.

From the frenulum, the lymphatics ascend circumferentially around the coronal sulcus, forming one to major collecting trunks dorsally that run proximally beside the deep dorsal veins to the suspensory ligament of the penis. At the level of suspensory ligament, these lymphatics anastamose with each other and creates the presymphyseal plexus, which drains to the superficial inguinal nodes.

The lymphatics of the prepuce, both inner and outer surfaces and of the penile skin converge on the dorsum of the penis and form several trunks that run to the base of the penis, where they desiccate and drain into superficial inguinal nodes. These anastamosis place the patient at risk for bilateral nodal involvement.

INNERVATION

Penis is supplied with both somatic and autonomic nerves. Somatic nerves are from the spinal nerves s2-s4 through pudendal nerve. First branch of the pudendal nerve, the dorsal nerve of the penis, runs over the surface of the obturator internus muscle and under the levator ani on the medial side of the internal pudendal vessels and penetrates the urogenital diaphragm to reach the dorsum of the penis. Dorsal nerves continue along their respective dorsolateral penile surfaces, lateral to the dorsal artery. The main cutaneous nerve supply of the penis and scrotum originates from the branches of these dorsal nerves.

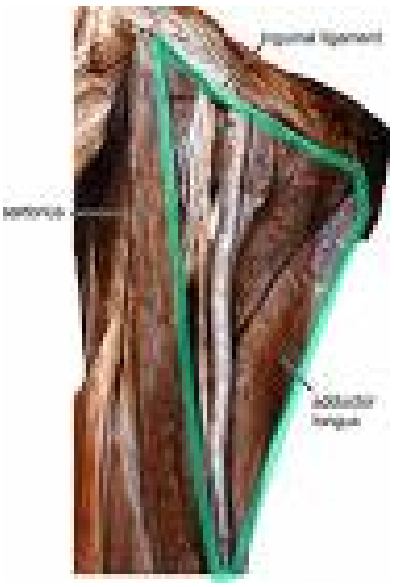
Autonomic innervations arise from the pelvic plexus, derived from fibers originating from the parasympathetic nerves S2,3,4 and sympathetic nerves T11-L2. Beyond the prostate, the parasympathetic nerves run adjacent to the membranous urethra, pierce the urogenital diaphragm and enter the corpora cavernosa.

ANATOMY OF THE GROIN

Since the treatment of carcinoma penis also involves the regional lymph node dissection, thorough anatomy of the groin is essential.

Inguinal lymph nodes are usually the first barriers against the lymphatic spread of the cancer metastasizing from the skin of the lower extremity and from the scrotum, labia, perineum, and perianal region, and umbilicus, infraumbilical part of the abdominal wall, clitoris, penis and glans. In addition inguinal nodes may receive metastases from prostate, urinary bladder, testis, epididymis, spermatic cord, ureter, kidney and urethra [(9).] Groin dissection has become the integral part of urologic surgical management of these malignant diseases.

FEMORAL TRIANGLE



BASE OF FEMORAL TRIANGLE

WARTY GROWTH

FEMORAL TRIANGLE (SCARPA'S TRIANGLE)

Inguinal ligament forms the base of the triangle. Sartorius forms the lateral border and adductor longus forms the medial border, apex pointing downwards. Floor of the triangle is formed from lateral to medial by iliacus, psoas major and sometimes a small part of adductor brevis. Fascia lata covers the triangle leaving a small opening – fossa ovalis, through which the long saphenous vein enters the femoral vein. Femoral vessels pass from the middle of the base of the triangle to its apex. For the first 4 cm, these vessels are surrounded by the femoral sheath, formed by extensions of the abdominal fasciae that pass under the inguinal ligament.

The femoral sheath has two partitions dividing it into 3 compartments. The lateral most contains the femoral artery. Intermediate compartment contains the femoral vein. Smaller medial compartment is called the femoral canal and contains fatty areolar tissue in which lies the node of cloquet or node of Rosen Muller.

Femoral canal is reported to be present only in humans where it has a protective function. On standing upright, the femoral vein expands suddenly and the femoral canal protects the vein from the sharp edge of lacunar ligament. Femoral nerve lies outside the femoral sheath. Femoral artery is the continuation of external iliac artery and continues as popiliteal artery at the opening of adductor magnus at the junction of middle and lower thirds of the thigh.

Within the femoral triangle, femoral artery gives many branches. The most important of them are superficial epigastric, superficial circumflex iliac, superficial external pudendal and the deep femoral (profunda femoris) artery. Other branches supply the sartorius, vastus medialis and adductor muscles.

The deep femoral artery arises from the lateral and posterior part of femoral artery 2.25 – 5 cm below the inguinal ligament. It can also originate from the external iliac artery or from medial or posterior part of femoral artery.

INGUINAL LYMPH NODES

Inguinal lymph nodes are grouped in many ways. Some investigators separate the nodes by a horizontal line that crosses the thigh at sapheno femoral junction. Those nodes above the line are termed “superficial inguinal”. Those below are called “sub inguinal nodes”. The Sub inguinal nodes are further sub classified into superficial (those above the fascia lata) and deep nodes (those beneath fascia lata). This classification is cumbersome and the common classification is based on that suggested by Rouviere [(12).] Based on this, inguinal nodes are of two types: superficial and deep.

SUPERFICIAL INGUINAL NODES

Inguinal region consists of 4-25 nodes. On an average, 8 nodes are present. In the absence of infection or malignancy, their size varies with the number. These group of nodes were originally thought to be bounded by the inguinal ligament above, the intersection of sartorius & adductor longus below, vertical line from anterior superior iliac spine laterally and another vertical line from pubic spine medially[(13).]

But after about 450 dissections by Daseler and associates, these boundaries were modified. The nodes were encased in a quadrilateral area bounded superiorly by a line 12 cm long and parallel to and 1 cm above the inguinal ligament and beginning medially just above the pubic tubercle; medially by a line 15 cm dropped perpendicularly downward from pubic tubercle; laterally 20 cm long line dropped

from the lateral limit of superior boundary and inferiorly transverse line 11cm connecting the lower limits of medial and lateral borders.

Quenu divided the superficial inguinal nodes into 5 groups by horizontal and vertical lines through saphenofemoral junction dividing the superficial nodes into superomedial, superolateral, inferomedial and inferolateral and a fifth group in front of long saphenous vein.

SUPEROLATERAL

- Skin of upper gluteal region
- Lateral posterior abdomen below the umbilicus
- Occasionally penile skin or prepuce , clitoris

SUPEROMEDIAL

* Umbilical and infra umbilical portion
* Vulva and parts of external genitalia
* Prepucium clitoritidis
* Cutaneous anal area
* penile skin
* perineum
* scrotum

Within this group lies the sentinel lymph node of Cabanas [14] [15].

INFEROMEDIAL

(usually absent)

* Medial aspect of thigh, leg and foot
* Penile skin, prepuce
* Cutaneous anal area
* skin of perineum
* scrotum, vulva
* rarely glans penis

INFEROLATERAL

- skin of anterior, lateral and posterior surfaces of thigh, leg and foot
- skin of caudal portion of gluteal region occasionally skin of perineum

CENTRAL GROUP

- usually a single node
- drain skin of scrotum, penis and vulva and from other zones

An additional node, the prepubic node may rarely be present anterior to pubic symphysis and carry metastasis from penis or clitoris and drain into superficial inguinal nodes.

From superficial nodes, lymphatics drain into deep nodes or directly into ext iliac nodes.

DEEP INGUINAL NODES

* Located under the fascia lata and medial to femoral vein. Usually 1-3 in number

* Constant of them is node of Cloquet or Rosen Muller located in the femoral canal.

* Lymphatic drainage almost always involves the superficial inguinal nodes and then drains into external iliac nodes. Direct drainage to pelvic nodes skipping the superficial nodes may also occur.

INCIDENCE AND EPIDEMIOLOGY

Carcinoma penis constitutes <1% of all cancers in the males in developed countries like US and 2% of urogenital cancers are carcinoma penis. The incidence is high in uncircumcised populations, where the incidence is 10 – 12% [16]. Penile cancer is the most common genitourinary cancer in Paraguay representing 45% - 76% of all genitourinary malignancies [17]. In Uganda, where circumcision is not practiced, penile cancer is the most commonly diagnosed cancer in males [18]. The incidence rate of ca. penis in US is 1 case per 100000 men [19] [20]. The incidence of penile cancer in a particular area or population is clearly influenced by cultural or religious practices and hygienic standards [21]. In under developed countries, the incidence is 15%-20% [1].

AGE:

* The incidence of penile cancer increases with advancing age in all populations
* But in areas of high incidence, earlier age of onset has been reported
* Patients tend to be 50 – 70 years of age in developed countries.

ETIOLOGY

1. PHIMOSIS AND CIRCUMCISION

Retention of prepuce after new born period is an important factor in etiology [22]. The incidence of penile cancer among uncircumcised population is thousand times higher than where newborn circumcision is the rule. However, circumcision after newborn period is less protective.

Wolharst in 1932 was the first to indicate that neonatal circumcision has a protective effect. Other benefits of circumcision are prevention of urinary tract infection in infant boys and of sexually transmitted diseases in young men. Uncircumcised men appear to be more susceptible to sexually transmitted diseases that disrupt epithelial surfaces such as genital herpes, syphilis, condyloma acuminata and chancroid [23][24][25].

Maden and associates showed the risk of penile cancer as 3.2 times greater among men who had never been circumcised relative to men circumcised at birth and 3 times greater among men who had been circumcised after the neonatal period.

2. SMEGMA

Smegma, a product of bacterial action on desquamated epithelial cells is carcinogenic in animal systems, although the specific component responsible for malignant degeneration in human males has not yet been identified. Among men not circumcised at birth, the relative risk associated with the presence of smegma was 2.1 times higher in Maden et al study.

3. HPV

Human papilloma virus is a double stranded DNA icosahedron containing approximately 8000 base pairs. [26] The use of polymerase chain reaction (PCR) and in situ hybridization (ISH) has helped to define the association of HPV with subsequent development of premalignant and malignant lesions of the penis. More than 65 types of HPV have been identified [27]. The HPV that

infect the anogenital area can be separated into two different groups on the basis of their association with recognized clinical entities [28]

The first group including HPV 6&11 is generally associated with benign condylomata, which are not associated with the subsequent development of penile cancer and are referred to as "low risk " viruses [28][29]. The "high risk "group including HPV 16 &18 is associated with premalignant and malignant lesions of the cervix [28], [29], [30]. Cloned viral genomes from high risk HPV s have been showed to transform cells in culture, a finding suggesting that those papilloma virus types may play an etiologic role in the development of these tumours [29]. In an examination of 30 specimens of penile cancer from 23 patients by PCR analysis, HPV 16 genome was found in15 patients (65%), HPV 30 was found in 3 (13%) and HPV 6 or HPV 11 in 2 (9%). Similar study was also reported from Japan.

These investigators demonstrated HPV 16 in a lymph node metastasis of penile cancer, the same HPV type as found in the primary tumour. A study by Sarkar and his associates confirms a strong association of presence of HPV 16 DNA and the bowenoid forms of intraepithelial neoplasia characteristic of carcinoma in situ of both cervix and the penis as well as invasive carcinoma of these organs.

In summary, advances and techniques in molecular biology have shown an ever increasing association between infection with certain HPV sub types and the development of both penile and cervical cancer. This finding may explain the strong association of premalignant and malignant changes of the penis in men with large number of sexual partners. Common

epidemiological factors in men that are associated with increased incidence of penile cancer, such as phimosis or chronic inflammation of penis, may actually indicate a higher risk of HPV infection and subsequent malignant cellular transformation.

4. OTHER FACTORS

- Smokers had a 2.8 times increased risk when compared to non smokers in Maden & associates study.
- Condyloma acuminata or penile warts showed 5.9 times increased risk.
- Leucoplakia of glans penis.
- Multiple sexual factors.
- History of penile tear or rash.
- Syphilis and gonorrhea have been implicated, but persistent etiologic relationship is yet unproven.

PATHOLOGY

Penile carcinoma is most often squamous cell in origin, although malignant melanoma, basal cell carcinoma, Bowen's disease (carcinoma in situ), mesenchymal tumors (including Kaposi sarcoma), adenocarcinoma (from Tyson's glands), metastatic lesions and leukemia or lymphomatous infiltrates may involve the penis. Several premalignant lesions have been identified and are shown below.

ERYTHROPLASIA OF QUEYRAT

LEUKOPLAKIA

lesion	characteristics	treatment
Leukoplakia	White plaque	Local excision
Erythroplasia of Queyrat	Raised, red velvety lesion cellular disorientation with multiple mitosis identical to ca. in situ of skin	Local excision Topical 5 FU Radiotherapy
Bowen's disease	Red plaque	Local excision
Balanitis xerotica obliterans	Scaly atrophic with ulceration meatus often involved	Local excision Topical steroids

CLASSIFICATION OF PENILE MALIGNANCIES

1. PRIMARY

EPITHELIAL:

1. Squamous cell carcinoma and its variants
2. Carcinoma in situ
3. Basal cell carcinoma
4. Adenosquamous
5. Merkel cell carcinoma
6. Adenocarcinoma

NON EPITHELIAL:

1. Melanoma

2. Sarcoma

2. METASTATIC

1. SQUAMOUS CELL CARCINOMA

(More than 95% of all penile malignancies)

Grossly, the tumors appear as moderately well demarcated firm, centrally ulcerated masses. Histologically, approximately 50% of lesions are of low grade and infiltrate the underlying tissues in finger like projections often appearing as nests and cords in tissue sections [39]. Keratin pearls are identified in infiltrative areas. Depending on the degree of differentiation, the individual tumor cells may be delineated by intercellular bridges. The nuclei are pleomorphic with coarsely granular, irregularly distributed chromatin. Many nuclei have one or more prominent nucleoli. Mitoses are easily identified. Advancing tumor margins are surrounded by a dense, predominantly lymphocytic infiltrate.

2. VARIANTS OF SQUAMOUS CELL CARCINOMA

A) VERRUCOUS CARCINOMA [40] (Giant condyloma of Buschke-Lowenstein)

This variant differs in following aspects.

- predominantly papillary configuration
- superficial “broad-front” invasive pattern
- minimal cytologic atypia
- metastasis uncommon

Verrucous carcinoma accounts for 5-16% of all penile malignancies [41]. They are distinguished from genital warts by their ability to invade and destroy adjacent tissue rather than their cytology [42]. Pseudoepitheliomatosis, micaceous and keratotic balanitis, originally considered as benign condition [43] is currently classified as variant of verrucous carcinomas [44]. This lesion lacks papillomatosis but has acanthosis, hyperkeratosis, increased mitosis, nuclear atypia, and a tendency towards recurrence and sarcomatous differentiation [45].

PEARLY PENILE PAPULES

CARCINOMA PENIS

B) SPINDLE CELL CARCINOMA (SARCOMATOID CARCINOMA)

This is a rare variant of squamous cell carcinoma in which lesions appear as polypoidal masses on glans penis [46]. Although thorough sampling has revealed areas of squamous differentiation, they are predominantly composed of spindle shaped cells embedded in a loose myxomatous stroma. These lesions tend to grow locally and appear to have a relatively favorable prognosis.

B) BASALOID CARCINOMA

This lesion resembles that of similar lesions of vulva and identifies a penile cancer with aggressive behavior.

3. CARCINOMA IN SITU:

This describes an intraepithelial neoplasm that may occur at various sites on the penis. When the lesion occurs on the glans, it is called Erythroplasia of Queyrat [18]. Lesions appearing on skin of prepuce or penile shaft are called Bowen's disease while those appearing as multiple nodules on the penile shaft are designated Bowenoid Papulosis [48] [49]. Erythroplasia and Bowen's are considered part of spectrum of squamous cell carcinoma. HPV DNA, type 16 has been documented in nearly every lesion [50] [51].

Cytologically these lesions have acanthosis with widespread replacement of normal epithelium by anaplastic cells that have large nuclei surrounded by scanty cytoplasm. Cells with multiple nuclear lobes or nuclei with folded and flat surfaces are frequently encountered and occasional cells have perinuclear halos. Isolated cases of Paget's disease and malignant penile horn the penis have been reported [52]. Paget's disease may also spread widely to involve skin of perineum, scrotum, groin and adjacent areas. Paget's may also be associated with previous transitional cell carcinoma of urinary bladder [53].

4. OTHER RARE CARCINOMAS

These include basal cell, inflammatory, adenosquamous, Merkel cell and adenocarcinoma [54]. Basal cell carcinomas can arise from penile shaft. The inflammatory and merkel cell cancers are aggressive. Isolated cases of skin appendage carcinomas have been reported [55].

5. MELANOMA

Melanomas are one of the more frequently occurring non-squamous cell malignancies of the penis [56]. Most are deeply invasive at diagnosis and the prognosis is poor. Melanomas occur in the same distribution as carcinomas (glans> prepuce> coronal sulcus)

6. NON EPITHELIAL NEOPLASMS

Cases of osteosarcoma, chondrosarcoma, endodermal sinus tumor and leukemic and lymphomatous involvement of the penis have been reported [57].

7. METASTATIC TUMOURS:

Metastatic cancer involving the penis is a rare phenomenon despite the fact that the organ has a rich blood and lymphatic supply and is in close proximity to the bladder, prostate and rectum. Metastatic lesions usually fill the corpora cavernosa; small solitary metastases are less common. The most frequent primary sites are bladder, prostate, rectum, kidney, colon, urethra, testis, lung, pancreas, ureter, bone and upper respiratory tract. Five modes of metastasis to the penis have been described:

1. Retrograde venous dissemination (most common)
2. Retrograde lymphatic dissemination
3. Arterial dissemination
4. Direct extension
5. Perineural tumor infiltration

These patients present with pain, swelling, priapism or alterations in voiding.

GRADING:

Most authorities agree that grading has practical value. The most popular scheme employs three grades, the lowest grade being the best differentiated [83]. Exact histological criteria that will allow most pathologists to reliably separate various grades of squamous cell carcinoma have not been adequately defined and disseminated. Grading has been justified because of its predictive value for regional lymph node metastases. Invasive penile carcinomas with grades other than 1 (well differentiated) have concomitant regional metastases in 80 – 100% of cases. Even so, approximately 50% of grade 1 tumors have concomitant nodal metastasis.

BRODER'S GRADING OF SQUAMOUS CELL CARCINOMA:

GRADE	DIFFERENTIATION	HISTOLOGICAL FEATURES
Grade I	Well differentiated	*prominent intercellular bridges * prominent keratin pearls * minimal atypia * rare mitotic figures
Grade II / III	Moderately differentiated	* occasional intercellular bridges * few keratin pearls * greater nuclear atypia * increased mitotic figures
Grade IV	Poorly differentiated	* marked nuclear pleomorphism * numerous mitotic figures * lymphatic invasion * necrosis, no keratin pearls * vascular invasion

CLINICAL FEATURES

Symptoms and signs associated with carcinoma penis are

1. ULCER

Patients usually present with an ulcer with indurated base most commonly over the glans prepuce or coronal sulcus in that order. This ulcer is usually painless. The lesion may be super infected

2. SWELLING

Patients may present with a proliferative mass. There may be ulceration and bleeding over the swelling. The swelling may be a small nodule or a papillary growth. The site of the lesion, either an ulcer or a swelling is usually the glans. In a review of larger series of penile cancer [62] the site distribution was found to be as below

Glans	48%
Prepuce	21%
Both glans and prepuce	9%
Coronal sulcus	6%
Shaft	2%
Invasion of shaft from more distal sites	14%

As the lesion grows, it develops one of two typical growth patterns: exophytic or ulcerative. Exophytic or papillary tumors generally have a better prognosis than flat or ulcerative lesions because the latter tend to infiltrate more deeply and are less differentiated than exophytic tumors [64, 65]. Characteristics of penile cancer that should be observed are the tumor configuration, size, location and fixation to the underlying Buck's fascia, induration in shaft.

3. INGUINAL LYMPH NODES

Patients may present with coexisting nodal mass in the groin or sometimes with nodes alone drawing the attention of the patient and the primary being hidden under phimosed foreskin. The inguinal areas in all cases of ca. penis should be palpated bilaterally to assess the nodal status and they should be mapped on the patients' records for comparison with subsequent examinations. A '50% rule' is applied here. 50% of cases of ca. penis have palpable nodes and among them 50% turn out to be malignant proved pathologically and the remaining 50% inflammatory.

In contrast 20 – 30 % of patients without palpable inguinal nodes may harbor occult metastases. This percentage varies significantly with the severity of the primary tumor.

The skin of the penis and lymphatics from the prepuce drain into superficial inguinal lymph nodes. Bilateral drainage occurs as a result of freely anastamosing system and cross over at the base of the penis. The glans is drained by the superficial inguinal lymph nodes but along with those of the corpora, the lymphatics of glans empty into deep inguinal and iliac nodes. The superficial lymphatics drain into the deep lymphatics and then to the external iliac, common iliac and para aortic nodes. Tumor invasion of the posterior may lead to deep pelvic nodes and internal iliac and obturator nodes.

4. PAIN

5. URINARY RETENTION / URINARY FISTULA – Rare

6. BLEEDING

7. SYSTEMIC SYMPTOMS :

Weight loss, weakness, fatigue, malaise can occur

8. DISTANT METASTASIS

Despite the rich vascularity of the corpora cavernosa, hematogenous spread is rare. Most tumors are disseminated through the inguinal and iliac nodes. Complications of treatment are more related to local recurrence and presence of bulky regional lymph node metastases than to wide spread dissemination of the disease. Distant metastases may occur in the lungs and bones. Only about 5% of penile cancer patients have distant metastasis at the time of diagnosis [80, 81, 82].

9. NON SPECIFIC PRESENTATIONS

Anemia

Hypercalcemia - More frequently associated with advanced stages.

INVESTIGATIONS

1. GENERAL INVESTIGATIONS:
    * Renal function tests, blood sugar, complete hemogram
    * Urine routine
    * ECG, CXR
2. SPECIFIC INVESTIGATIONS:
    * To confirm diagnosis
    * To stage the disease
3. OTHER NON SPECIFIC INVESTIGATIONS:
    * Serum calcium
    * Serum proteins
    * Serum alkaline phosphate

1. WEDGE BIOPSY

In case of primary presenting as an ulcer, a wedge biopsy is taken from the edge of the ulcer as distally as possible and sent for histological examination. The pathological features that are expected in carcinoma penis are already discussed under the section "Pathology". The wedge should include a portion of normal tissue because the malignant potential of a lesion can be observed by assessing the cellular interaction of the tumor with normal adjacent tissue and the nature and extent of invasion. Similarly, a biopsy should be deep enough to determine the lesions depth of penetration of underlying tissue.

2. ULTRASONOGRAPHY

Helps to assess the corporal involvement in penile cancer[90]. Although this technique has had limited use in this manner, its ease of application, non invasiveness and low cost may make ultrasonography a useful diagnostic modality in staging penile cancer.

3. COMPUTED TOMOGRAPHY

Computed tomography has not been shown to have any practical use in assessing the primary lesion in penile cancer because it does not enable the clinician to distinguish tumor from adjacent corporal tissue [92]. However, CT is the most popular imaging technique for the detections of lymphadenopathy [92, 93, 94, 95]. Identification and evaluation of the pelvic nodes may be more difficult than assessing para aortic nodes, because of the relative scarcity of fat enveloping the pelvic nodes and their oblique orientation. Further more, CT can only detect non specific lymph node enlargement. Nonetheless, this study is done routinely to determine the status of the pelvic nodes even in the absence of inguinal adenopathy.

4. MRI

Magnetic resonance imaging is very useful in determining the extent and stage of the primary lesion [93, 94]. Advantages include superior contrast and imaging in multiple planes. Studies of the normal penis have shown that the tunica albuginea enveloping the corpora has low signal intensity and the contrast between the tunica and the corpora is increased on T2 (transverse) weighted images [94, 95]. Buck's fascia is indistinguishable from the tunica on T2 weighted images but the two may appear as separate structures on T1 (longitudinal) weighted images [95].

MRI may also be used to assess the status of both inguinal and pelvic nodes in patients with penile cancer, although experience with this modality is limited [92-95]. Although it has advantages of scanning in multiple planes, MRI also depends on enlargement of the lymph nodes in defining abnormality, and does not enable one to disseminate tumor from other cases of nodal enlargement [95]. For these reasons, MRI imaging does not offer any clear advantage over CT in the evaluation of patients with nodal involvement in penile cancer.

5. FNAC

This is an ideal investigation in the staging of penile cancer because the lymph nodes are readily accessible and aspiration of the lymph nodes can be done under direct vision. An ideal use of FNAC would be in the patient who has negative or equivocal nodes at diagnosis and who has significant contraindication to inguinal node dissections, such as obesity, previous pelvic surgery or a history of cardiac or thrombo embolic disease. Negative results of fine needle aspiration of the inguinal lymph nodes would be reassuring when observation of the inguinal area is contemplated. FNAC when combined with imaging techniques enhances the diagnostic accuracy of those tests. With further advances in imaging techniques, fine needle aspiration may play more roles in patients with penile cancer in the future.

6. SENTINEL NODE BIOPSY

Ramon Cabanas in 1968, introduced the concept of sentinel node during his work on Carcinoma of penis. Later on, this concept was extended to breast, melanoma, rectum etc [97]. Based on previous lymphangiographic studies, cabanas defined the sentinel node as the primary site of metastasis for penile cancer, and this node is located on the anteromedial aspect of the superficial epigastric vein medial to and above the epigastric-saphenous junction. In his original series, cabanas reported that inguinal lymph node metastasis were absent in patients with negative sentinel lymph node biopsy and 80% of patients with a positive sentinel lymph node had no other nodal involvement, whereas regional spread was documented in the remaining 20%. However, Perinetti and colleagues [98] have reported patients with negative sentinel node biopsies who later developed unresectable bilateral groin disease.

STAGING OF CARCINOMA PENIS

I. JACKSON'S STAGING SYSTEM (1966):

Stage I	Tumors confined to glans, prepuce or both
Stage II	Tumors extending into the shaft of penis
Stage III	Tumors with operable inguinal metastasis
Stage IV	Tumors associated with inoperable inguinal or distant metastasis

II. AJCC STAGING SYSTEM

From American joint committee on cancer [100], 1989.

T	N
Tx – primary tumor cannot be assessed	**Nx –** regional lymph nodes can't be assessed
To- no evidence of primary tumor	**No** – no regional lymph node metastasis
Tis- carcinoma in situ	**N1-** metastasis in a single superficial lymph node
T1-tumor invades subepithelial connective tissue	**N2 -**metastasis in multiple or bilateral superficial inguinal lymph nodes
T2- involves corpus spongiosum or cavernosum	**N3-** metastasis in deep inguinal or pelvic nodes. Unilateral or bilateral
T3 -tumor involves urethra / prostate	
T4- tumor involves adjacent organs	

Mx – Presence of metastasis cannot be assessed.

Mo -- No distant metastasis

M1 – Distant metastasis

III. UICC STAGING SYSTEM (UNION INTERNATIONALE CENTRE LE CANCER)

T (Tumor)

T o - None

Tis - Carcinoma in situ

T1 - Superficial, exophytic ≤2 cm

T2 - Minimal infiltration 2-5 cm

T3 - > 5 cm, deep invasion, including urethra

T4 - Invasion of adjacent structures

N (Nodes)

No - None palpable

N1 - Unilateral mobile

N2 - Bilateral mobile

N3 - Fixed

M (Metastasis)

M0 - None

M1 - Metastasis present, any site

MANAGEMENT

Treatment depends on the local extent of the primary lesion and the status of the regional lymph nodes. Treatment comprises of

1. Treatment of primary lesion

2. Management of regional lymph nodes

The options for primary are

1. Surgery
2. Radiotherapy
3. Chemotherapy
4. Combined

TREATMENT OF PRIMARY LESION

SURGERY

Management of primary lesion involves total removal of the lesion with adequate tumor free margin, with the least possible cosmetic and functional loss. Therefore, surgery remains an important element in the management of penile cancer. Partial or total penectomy remains procedure of choice in bulky, exophytic penile cancer, which continues to be evident at diagnosis in many cases.

CIRCUMCISION:

Circumcisions appear to have a fairly limited role as the sole treatment of penile cancer, because recurrence rates of 32 to 50% have been reported [109) (110) (111)]. For superficial lesions limited to the foreskin, however circumcision would appears to be an ideal form of management. Careful attention to the margins is necessary when circumcision is performed and it is helpful to mark the specimen clearly to assist the pathologist in examining the most critical margins

PARTIAL PENECTOMY:

Partial penectomy is indicated for lesions that because of their size, invasiveness or location on the shaft are not amenable to more conservative treatment.

Partial penectomy must ensure adequate penile length for voiding in upright position. If the stump is too short it may be engulfed by the groin pad of fat and the patient ends dribbling urine down both legs. Partial penectomy includes a 2 cm margin of normal shaft proximal to primary tumor and a stump of at least 3 cm should be present.

TOTAL PENECTOMY:

Where partial penectomy is not possible, total penectomy is accomplished with excision of both corpora and creation of a perineal urethrostomy.

PENILE RECONSRUCTION AFTER TOTAL PENECTOMY:

Borgoras was the first to report penile reconstruction in 1936. He used tubed abdominal flaps with ribbed cartilage for rigidity. Other techniques that have been used are local tubed pedicle flaps and skin flaps, muscle and myocutaneous flaps, local fasciocutaneous flaps, and more recently sensate, fasciocutaneous microvascular free flaps [112].

A fasciocutaneous forearm free flap is the usual tissue donor site, elevated on either the radial or ulnar artery and is transferred to the recipient site by microsurgical anastamosis to either the inferior epigastric vessels or through a vein interposition graft to the superficial femoral artery. The medial or lateral antebrachial nerves are included in the flap for cooptation to the dorsal nerves of the penis.

REGIONAL THERAPY AND LYMPHADENECTOMY:

Factors considered while planning the management of regional lymph nodes:

- Firstly, involvement of lymph nodes is the single most important prognostic factor in cancer penis
- Lymph nodes dissection can be curative for the majority of patients with isolated tumor bearing inguinal nodes

These facts indicate that the management of the regional lymph nodes forms an integral part in management of cancer penis. However, only 50% of cancer penis patients have palpable

inguinal nodes at diagnosis, of which, 50% represent benign inflammatory changes associated with ulcerated or infected penile lesions.

Hence, lymphadenectomy is not necessary in all cases of carcinoma penis with enlarged nodes. This problem is overcome by assessing the nodes after 4 to 6 weeks course of antibiotic therapy. Persistent adenopathy after 6 weeks warrants biopsy and therapy.

But the primary controversy in the management of penile cancer concerns the role of lymph node dissection if there is no clinically identifiable inguinal disease.

- 20% of clinically non palpable nodes harbor occult metastasis

The management options available for such a group of patients are

1. Prophylactic lymphadenectomy in non palpable groups also, or,
2. Delay lymphadenectomy until clinically evident node involvement exists (therapeutic lymphadenectomy)

ADVANTAGES OF PROPHYLACTIC LYMPHADENECTOMY:

- If a prophylactic lymphadenectomy is done and microscopic metastasis are found pathologically, 84% survive 5 years where as in those patients in whom delayed lymphadenectomy is done, 8 – 42% survive 5 years. The cure rate therefore is much better if regional disease is removed when microscopic than palpable [(5).]
- Complications of groin dissection are much less in those receiving a groin dissection for microscopic disease compared with delayed dissection of nodes that are palpably positive at a later date [(113)].

In a report by Uehling, when delayed lymphadenectomy is opted, the most common cause of treatment failure was progression to inoperable nodes in 22% of patients monitored [114]. Studies have reported a significant decrease in 5 years survival rates in patients with therapeutic rather than prophylactic groin dissection and have suggested that delayed surgery is inappropriate [115].

Though these points favor a prophylactic lymphadenectomy for nodes not involved pathologically, this would lead to performance of such a dissection with survival benefit at a cost of increased morbidity.

If those patients without palpable lymph nodes who have microscopic nodal metastasis could be identified, they would certainly benefit from a lymphadenectomy. Methods to detect micro metastasis have not yet yielded consistent results. Some have suggested that a biopsy could provide information for making this decision. However, the experience of many is that lymph node biopsy carries a false negative rate if at least 50% [117]

Cabanas proposed that sentinel node biopsy would be helpful, but the lack of full follow up on some of the patients in that study [120] and the experience of many others suggest that this type of biopsy has a high rate of false negative results as well [121], therefore the use of regional biopsy to predict the presence of regional nodal disease does not appear appropriate.

Thus when it is not possible to detect microscopic disease in clinically non palpable nodes, another method to detect those patients who are likely to have microscopic disease should be adopted and selected for prophylactic nodal dissection, such as

1. Grade of the lesion (differentiation) &
2. Depth of invasion (T stage)

GRADE OF THE PRIMARY	RATE OF REGIONAL NODAL INVOLVEMENT
Poorly differentiated	82%
Moderately differentiated	46%
Well differentiated	24%

In one series, all patients who had poorly differentiated tumors developed regional metastasis [113]. The depth of invasion is also important in determining the likelihood of regional and distant metastasis. Lesions that do not involve the substance of corpus spongiosum or cavernosum have 5% - 11% rate of progression to regional disease [123,124]. These superficial penile lesions have a 92% survival rate at 3 years [123]. Since the differentiation of the primary lesion and the depth of invasion are important in predicting regional lymph node metastasis, a modification of Jackson system has been made to reflect current therapy. With this modification, appropriate determination of stage allows a reasonably certain prediction of the likelihood of positive regional lymph node involvement.

MODIFIED STAGING SYSTEM

STAGE I **:** superficial, does not extend to subcutaneous tissue: well differentiated

STAGE II A **:** locally invasive, without involvement of corpora: well or moderately differentiated

STAGE II B **:** Invasion to corpora: poorly differentiated

STAGE III **:** Palpable inguinal nodes that persist after 6 weeks of antibiotic therapy

STAGE IV **:** Inoperable groin nodes, iliac nodal involvement, and distant metastasis

SURVIVAL ACCORDING TO MODIFIED STAGING SYSTEM

STAGE	DISEASE FREE 5 YEAR SURVIVAL
I	**100 %**
II A	**100%**
II B	**90%**
III	**70%**

(All patients had a regional lymphadenectomy shortly after treatment of primary)

Thus the T stage of the primary and the grading play a crucial role in planning the management of the regional lymph nodes.

COMPLICATIONS OF REGIONAL LYMPHADENECTOMY

FLAP NECROSIS	5%
WOUND INFECTION	15%
LYMPHEDEMA LEGS/ SCROTUM	16%
LYMPHOCELE	9%
LOSS OF SKIN EDGES	30%
WOUND SEROMA	20 – 80%
THROMBOPHLEBITIS	
HAEMORRHAGE	
FEMORAL ARTERY BLOW OUT	

ORGAN SPARING SURGERY FOR CARCINOMA PENIS

For cancer penis, the issue of quality of life is measured in terms of functional and psychological morbidity [125,126,127]. Organ sparing dermatological surgical techniques are gaining acceptance. Use of these surgical techniques for local control, with an emphasis on Mohs Micrographic Surgery (MMS) is discussed.

MMS was first described in 1930's by a general surgeon at the University of Wisconsin, Fredrick E. Mohs. As a well established form of margin controlled surgery, the technique has been producing results unmatched by other modalities of treatment for cutaneous SCC. Rowe and associates demonstrated that MMS produces better results for cutaneous SCC than all other modalities. Mohs demonstrated MMS to give 94% cure rate in 31 patients of Jackson's I –III. For treatment of penile SCC, MMS produces impressive long term cure rate and compares favorably with the more disfiguring technique of partial penectomy [129].

ORGAN SPARING SURGICAL TECHNIQUES

1. Laser ablation
2. Circumcision
3. Wedge resection
4. Frozen section guided ellipse excision

Frozen section controlled techniques are of two types:

1. standard
2. Mohs

Standard excision and Mohs are different in the way in which surgical specimens are pathologically processed. This is very important regarding the quality of margin control.

Mohs is done as an outpatient procedure using local anesthesia. The overall procedure is composed of a series of excisions and pathologic tissue processing described in stages. In stage one; the clinically evident tumor is surgically debulked. A two dimensional diagram, "the Mohs map" drawn of the specimen relates its orientation to the surgical defect. The concept of orienting the tissue specimens horizontally which allows for review of 100% of the surgical margins, is unique and is what sets MMS apart from all other techniques of skin cancer removal. In addition, the Mohs surgeon does the excision and interprets the pathological specimens, thereby further enhancing maintenance of appropriate orientation of tissues.

TREATMENT OF PRIMARY PENILE CANCER <3.5 CM IN DIAMETER

JACKSONS STAGE UICC / TNM	**WELL DIFFERENTIATED**	**MODERATELY DIFFRENTIATED**	**POORLY DIFFERENTIATED**
I (Tis,T1-2,No,Mo)	MMS	MMS	MMS
II (T3-4,No,Mo)	MMS	MMS	PP/MMS
III(T1-4,N1-3,Mo)	PP/MMS	PP/MMS	TP/MMS

(MMS-Mohs micrographic surgery; PP-Partial penectomy; TP-Total penectomy)

ROLE OF RADIOTHERAPY IN CARCINOMA PENIS

The principle advantage of radiotherapy is its organ sparing cure with maintenance of function. The functional and psychological consequences of undergoing penectomy, whether total/ partial can be devastating, particularly in younger patients, and the psychological need for normal urinary and sexual function should not be underestimated in the elderly.

The role of radiotherapy involves

1. Treatment of primary
2. Treatment of regional lymphatics

Before radiotherapy, circumcision should be performed both to assess the extent of tumor and to minimize the morbidity associated with radiotherapy. Infection, which can happen secondary to tumor, should be treated as it increases radio resistance. [133] Fibrosis of the foreskin occurs as a late complication, causing an inability to retract the foreskin and impede sexual function. In addition, follow up care is better facilitated by the absence of the foreskin, which allows for a more thorough tactile and visual examination.

RADIOTHERAPEUTIC METHODS:

1. Superficial X rays
2. Teleradium sources
3. Megavoltage gamma and x rays
4. Interstitial implants with Iridium 192
5. Interstitial and contact brachytherapy
6. External beam radiation
7. Electron beams

EXTERNAL BEAM RADIOTHERAPY (EBRT)

Most radiotherapy departments have used Cobalt-60 or 4MV photons with appropriate bolus. Most series have treated patients to a total dose of 50-60 Gy in fractions of 2-3.5 Gy through parallel opposed fields. Several devices have been designed to achieve a homogenous dose like molded wax bolus, plastic box with central opening, water filled containers, Perspex tube etc. Bowen's disease and Erythroplasia of Queyrat which are typically treated with local excision or topical 5 FU may respond well to irradiation.

External beam radiotherapy can be combined with concurrent chemotherapy. Most commonly used chemotherapeutic agents are Bleomycin either alone or with Methotrexate [135]

COMPLICATIONS OF EBRT:

1. Dry or moist desquamation
2. Atrophy of penile skin
3. Urethral strictures
4. Radio necrosis of penis
5. Erythema
6. Swelling of penis
7. Impotence
8. Lymph edema of legs

BRACHYTHERAPY

Two types of brachytherapy used are:

1. Contact brachytherapy
2. Interstitial brachytherapy

In contact brachytherapy, the radioactive source is placed in contact with the tissues to be irradiated. In interstitial type, the radioactive sources are placed inside the tumor bed. Of the two, interstitial is used more often.

Sources used for brachytherapy are

* Cobalt 60
* Radium 226
* Tantalum 182
* Gold 190
* Iridium 192 - Iridium 192 is the most commonly used source.

* A dose of 60-65 Gy is delivered. Urethral dose is limited to 50 Gy. Gonads: 8-16 Gy

* The aim is to treat the tumor with margin of 2 cm proximal to the tumor and 1 cm distal to the tip of the penis.

METHOD: 1. INTERSTITIAL BRACHYTHERAPY

Under general/ spinal anesthesia, a Foley's catheter is inserted and left in place for the duration of treatment. A Plexiglas template is placed on each side of the penis and holes are drilled in a pattern to match the desired arrangement of the implant. Angiocatheters or hypodermic needles which are used as vectors for insertion of the radioactive sources are inserted in one or more parallel planes through the tumor bed, oriented perpendicular to the axis of the penis. The vectors may be spaced with an intersource distance of 10-22 mm. one end of the vector is sealed with lead and radioactive source is inserted and the other end sealed. A small sponge placed at the penile base elevates the penis and distance the testicles from radioactive sourced.

2. CONTACT BRACHYTHERAPY

This involves the use of surface mold containing radioactive sources that can be worn over the penis. A cylindrical plastic mold is fitted to the penis and an outer mold is constructed to slide over the inner mold. The applicator mold (outer mold) can be removed if the patient wishes to urinate and kept in lead container at the bedside. The application mold is left in place for 10-12 hrs per day over 7-8 days period.

CONTRAINDICATIONS TO BRACHYTHERAPY:

1. Tumor size > 4 cm
2. Major invasion of corpora cavernosum (> 1cm invasion)

In general, brachytherapy with surgical salvage in the event of failure has been shown to produce results equivalent to those of primary surgery, the principle advantage being sparing the organ and the psychological sequelae following that and the much shorter time of treatment than that of EBRT.

COMPLICATIONS OF BRACHYTHERAPY

1. Erythema
2. Edema of subcutaneous tissue
3. Urethral mucositis
4. Telangiectasia, dyschromia & superficial sclerosis
5. Urethral stenosis
6. Radio necrosis (occurs within 18 months after completion of treatment)

6% of Patients treated with brachytherapy required amputation for complications.

RADIOTHERAPY FOR REGIONAL LYMPHATICS

Comparison of survival rates in patients who underwent lymphadenectomy or radiotherapy for either prophylactic or therapeutic treatment of groin [137]

MODE OF TREATMENT (PROPHYLACTIC)	3 YEARS	5 YEARS
SURGERY	64%	50%
RADIOTHERAPY	44%	44%

MODE OF TREATMENT (THERAPEUTIC)	3 YEARS	5 YEARS
SURGERY	52%	34%
RADIOTHERAPY	27%	30%

Elective irradiation of clinically uninvolved groins, known to be of benefit for squamous cell cancers at other sites (eg. Head and neck, cervix) is of uncertain benefit for penile cancer. Patients who present with extensive or poorly differentiated tumors may benefit from elective groin irradiation. Both the inguinal and pelvic nodes should be treated. Megavoltage X rays using parallel opposed fields should be used. Weighted photons may also be used.

DOSE:

Prophylactic - 50 Gy

Therapeutic - 65-70 Gy

ROLE OF CHEMOTHERAPY IN CARCINOMA PENIS

Recently it has become possible to verify the reproducible efficacy of some combination regimes and to suggest a more rational use of chemotherapy in multimodality treatment. Combination chemotherapy is expected to improve cure rates in patients with nodal metastasis.

Indications for chemotherapy in carcinoma penis:

1. systemic therapy in rare cases of distant metastasis
2. Neo adjuvant chemotherapy for fixed inguinal nodes.
3. Adjuvant therapy after nodal resection.
4. As a combined modality of treatment in organ sparing therapy in selected cases.

Drugs used:

Single agent: Bleomycin

Methotrexate

Cisplatin

Combination chemotherapy:

1. **Alsarraf regimen:**Cisplatin + 5FU (PF)
2. Methotrexate + Bleomycin + Cisplatin (MBC)
3. Vincristine + Bleomycin + Methotrexate (VBM)

Combination chemotherapy achieves better results than single agent chemotherapy. Of the three regimes VBM is the easiest to administer. The two cisplatin containing regimens seem to be more effective and the MBC regimen is the most toxic. Alsarraf and VBM regimens provide better results.

DOSE:

PF (ALSARRAF) REGIMEN:

Cisplatin	100 mg/m^2 IV day 1
5 FU	1000mg/m^2 IV infusions daily 1-4 days

VBM REGIMEN

Vincristine	1 mg IV day 1
Bleomycin	15 mg IM 6 &12 hrs after Vincristine
Methotrexate	30 mg oral on day 3

MATERIALS AND METHODS

Analysis of 45 patients of carcinoma penis from the period of June 2005 to September 2007 at Government Royapettah Hospital & Kilpauk medical college, Chennai.

At presentation history is taken; relevant points are noted and staged. Biopsy is taken for pathological diagnosis and grade.

Clinical assessment of the regional lymph nodes is done and recorded. FNAC of the enlarged lymph nodes is done.

Investigations were done and patients were taken up for surgery. Surgery for the primary and nodes were recorded and the post surgical histopathology is obtained and patients followed up.

Patients presenting with inguinal nodes alone after primary surgery done at different places were also included retrospectively.

The data obtained were recorded in a specific proforma designed for the purpose and analyzed in a systematic way and conclusions drawn.

OBSERVATIONS AND DISCUSSION

Analysis of 45 cases from June 2005 to September 2007.

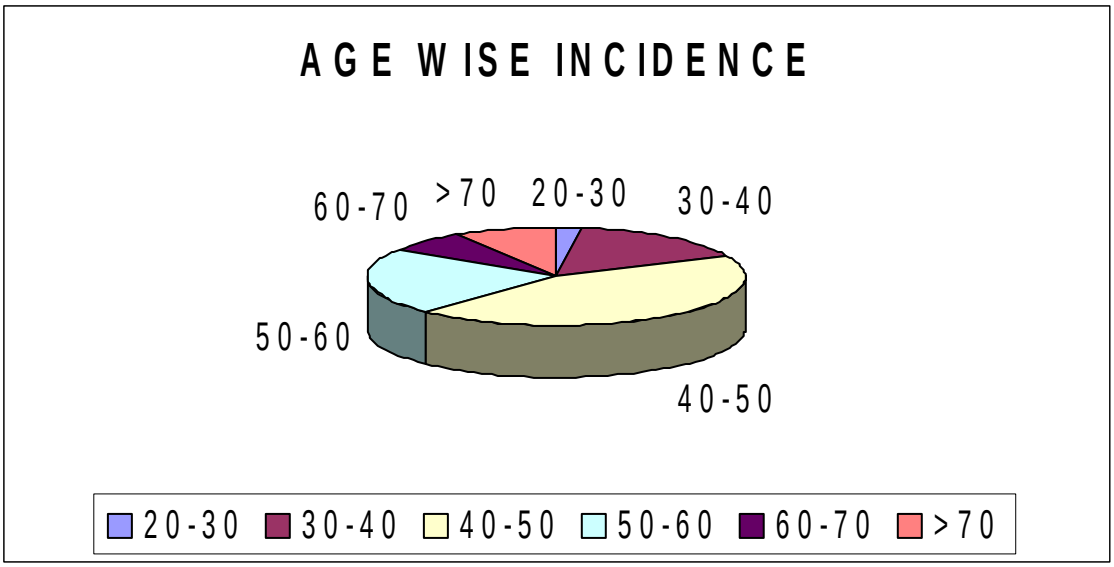
Definition of cases included only those confirmed to have squamous cell carcinoma of penis histopathologically

There was no uniformity in the therapy followed. Different plan of treatment depended on the T stage, grade of the tumor, presence of inguinal nodes and patient's general condition.

AGE WISE INCIDENCE:

OUR STUDY, GOVT. ROYAPETTAH HOSPITAL, KILPAUK MEDICAL COLLEGE, CHENNAI, JUNE 2005-SEP 2007		**FLETCHNER C DERRICK, MEDICAL UNIVERSITY OF SOUTH CARDINA, 1946-1966, JOURNAL OF UROLOGY; VOL 110**	
AGE	**NO. OF CASES**	**AGE**	**NO. OF CASES**
20-30	1	20-29	1
30-40	7	30-39	9
40-50	20	40-49	24
50-60	10	50-59	19
60-70	3	60-69	25
>70	4	70-79	7
TOTAL	**45**	80-89	2
		TOTAL	**87**
MODE	**45 YEARS**	**MODE**	**65 YEARS**

The age wise incidence in western studies show peak incidence in 60-70 years. In our study the peak incidence is 40-50 years.



COMPARISON OF AGE WISE INCIDENCE WITH WESTERN STUDIES

STUDY	AGE IN YEARS
Kamal A. Hanash, Minnesota (1945-1965)	68 years
Begg & Spratt (1961)	69 years
Hardnes (1970)	67 years
Our study (2005-2007)	45 years

This lower age incidence is due to the fact that in countries where the overall incidence of carcinoma penis is higher, the peak incidence is at lower age.

SYMPTOMS AT PRESENTATION

The commonest symptom of presentation in our report is Growth: 23 cases.

The other presenting symptoms were:

SYMPTOMS	NUMBER OF CASES	PERCENTAGE
Growth	23	51.1
Ulcer	20	44.4
Discharge	10	22.2
Groin mass	4	8.9
Urinary symptoms	3	6.7
Edema & inflammation	2	4.4

Hanash & Associates 1965

SYMPTOMS	NUMBER OF CASES	PERCENTAGE
Ulcer	66	39
Growth	67	39.6
Node	6	3.6
Discharge	21	12.4
Edema & cellulitis	9	5.3

DURATION OF SYMPTOMS:

Average duration : 9.5 months

Comparing age group and duration of symptoms

Age group	Average duration in months
20-30	6.7
30-40	10.2
40-50	9.6
50-60	8.9
60-70	10.4
>70	11.3

The average duration of symptoms in our patients is 9.5 months. In contrast the western studies show an average duration of symptoms to be less than 3 months.

Our patients ignore the symptoms for a long time. Patient with an ulcer and discharge come early than a patient with proliferative lesion.

Younger patients seek medical attention much earlier than older patients. No strict comparison was possible as the duration of symptoms depend on many factors like literacy, socioeconomic status, accessibility.

SITE OF ORIGIN:

The most common site of origin in our study is the Glans.

This result confirms the literature reports that glans is the most common site followed by prepuce, coronal sulcus and shaft, in that order.

SITE OF ORIGIN	NUMBER	PERCENTAGE
GLANS	26	57.8%
PREPUCE	12	26.7%
CORONAL SULCUS	6	13.3%
SHAFT	1	2.2%

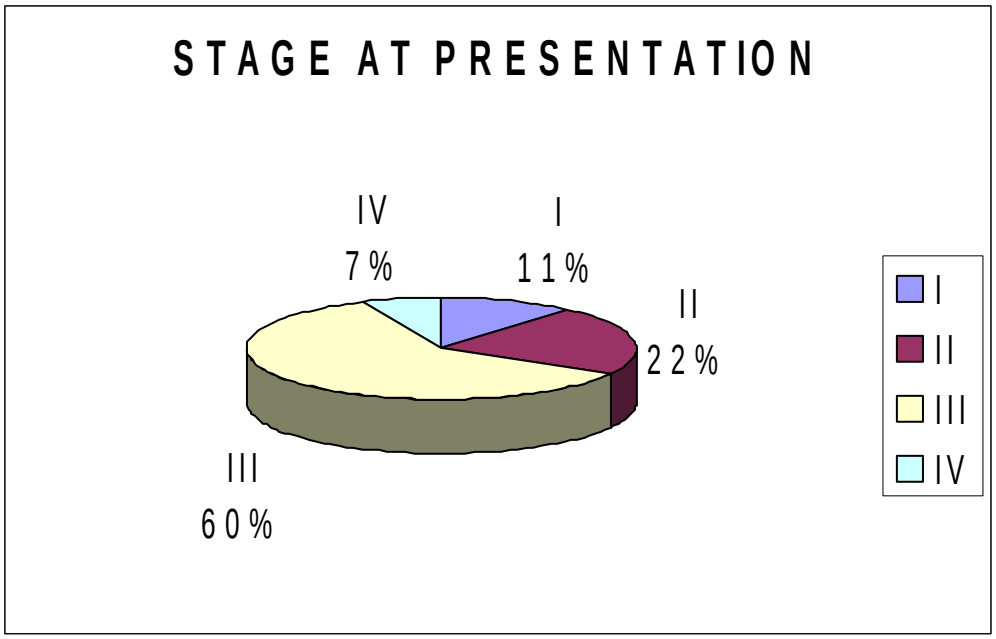
Comparing this with a review of large series of penile cancer by Sufrin G, Huben R (Ref: benign and malignant lesions of the penis. In Gillenwater Jyed Adult and pediatric urology 2nd edition Chicago year book 1991:1643)

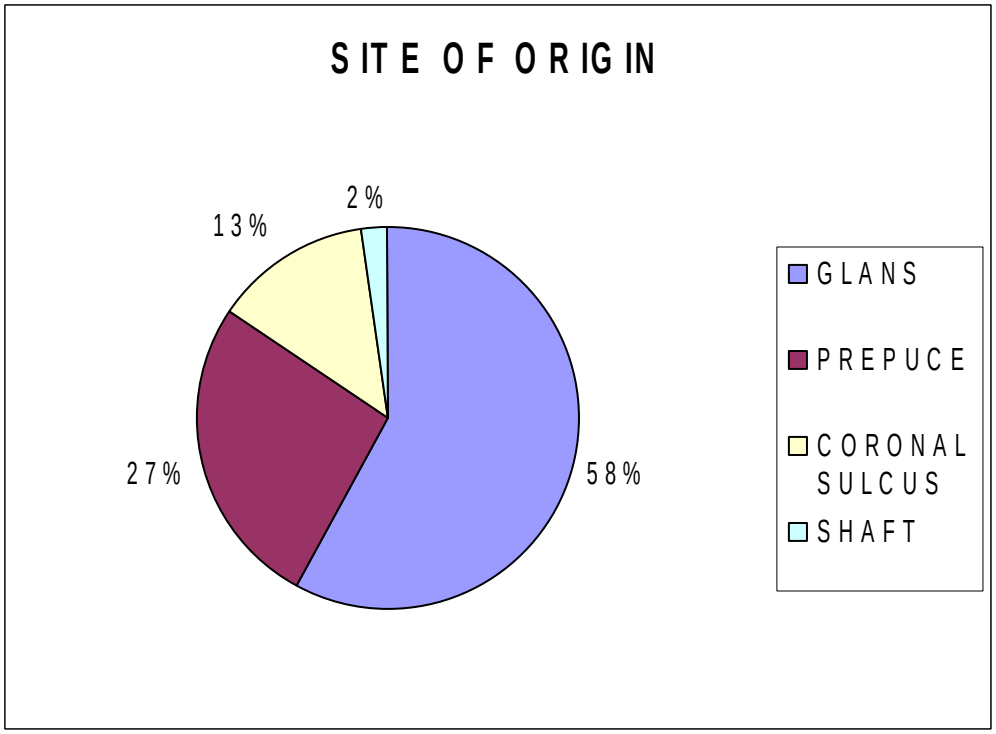
GLANS	48%
PREPUCE	21%
CORONAL SULCUS	6%
SHAFT	2%
BOTH GLANS & PREPUCE	9%

STAGE AT PRESENTATION:

In our study most of the cases presented at stage III

OUR STUDY			BARNES ET AL CAPETOWN, S.A,1968-85		
STAGE (JACKSON'S)	**NO.OF CASES**	**%**	**STAGE (JACKSON'S)**	**NO. OF CASES**	**%**
I	5	11.10%	**I**	27	44%
II	10	22.20%	**II**	17	27%
III	27	60%	**III**	12	19%
IV	3	6.60%	**IV**	6	10%


STAGE AT PRESENTATION
IV
7%
I
11%
II
22%
III
60%
I
II
III
IV


SITE OF ORIGIN
2%
13%
27%
58%
GLANS
PREPUCE
CORONAL SULCUS
SHAFT

ETIOLOGICAL FACTORS:

Analyzing the etiological factors of 45 cases studied, none of the cases occurred in circumcised penis. One patient reported history of cancer cervix in the sexual partner. Association of HPV and cancer penis could not be studied since HPV testing was not done in any of the cases.

History of recurrent preputial infection and history of STD was elicited in 3 patients. Again a strong relationship could not be documented as the number is small. Two of the cases reported having premalignant lesion- leukoplakia, on which the cancer occurred.

TYPE OF LESION:

The lesions were either ulcerative or proliferative. Ulcerative lesion was seen in 24 cases and proliferative in 21 cases. Ulceroproliferative cases were taken as proliferative lesions.

OUR STUDY		
ULCERATIVE	24	53.3%
PROLIFERATIVE	21	46.7%
TOTAL	45	100%

NODAL STATUS:

Of the 45 cases studied, 30 cases (67%) presented with clinically palpable nodes at presentation. But only 11 were positive (36.7%) by fine needle aspiration biopsy (FNAC). Of these 11, 3 were inoperable inguinal nodes and hence radiotherapy was given to them, and the other 8 cases underwent ilio inguinal block dissection at the first sitting. Remaining 19

clinically node palpable cases in which FNAC was negative were kept on follow up with antibiotics, of which 6 of them developed pathological positivity later. Altogether 17 cases (56.7%) developed pathological positive nodes among node palpable 30 cases. Remaining 13 cases (43.3%) remained inflammatory and regressed. This confirms with the reports in literature that approximately 50% of the clinically palpable nodes at presentation are inflammatory.

67%	Cases presented with palpable nodes
56.7%	Pathologically positive
43.3%	Regressed with antibiotics

Of the total 17 pathologically positive cases, initial FNAC was able to detect only 11 of it indicating its sensitivity to be about 65%.

Of the total 45 cases, 15 cases did not have clinically palpable nodes at presentation. But however in 3 cases, nodes appeared during follow up and were pathologically documented. When the patients presented with nodal metastasis, nodes were already fixed and inoperable and only salvage chemotherapy and radiotherapy could be instituted.

No. of cases	**%**	**Nodal status**
15	33.3%	Nodes not palpable
3	20%	False negative
12	80%	Negative nodes

Overall of the 45 cases studied, the nodal status is given below:

OUR STUDY:

NODES	CLINICALLY	PATHOLOGICALLY
POSITIVE	30	17
NEGATIVE	15	12

STUDY BY J.HARDENER

NODES	CLINICALLY	PATHOLOGICALLY
POSITIVE	48	20
NEGATIVE	52	38

Clinically positive nodes turning pathologically negative: 43.3%

Clinically negative nodes turning pathologically positive: 20%

Our study confirms the literature studies' that 50% of clinically palpable nodes are inflammatory and 20% of clinically negative nodes harbor occult metastasis. The number of inflammatory enlargement of nodes is slightly higher in our study compared to western study because of lack of personal hygiene and the secondary infection rate of the primary lesion is greater.

Comparison study

Kamal A et al 1965	:	58% nodes were pathologically -ve
Dr.N. Anandakrishan	:	50% Positivity
Begg and Spratt 1961	:	80% of clinically –ve nodes were pathologically -ve 20% of –ve nodes contained occult metastasis.

FACTORS ASSOCIATED WITH NODAL INVOLVEMENT

Only the pathologically involved nodes are taken up for analyzing the associated factors. Of the 17 patients who had pathologically positive nodes in our study, the underlying factors are individually analyzed.

Age:

Age	No. of cases	No. of node positive cases	Percentage
20-30	1	0	
30-40	7	2	28.5
40-50	20	9	45
50-60	10	3	30
60-70	3	2	66.7
>70	4	1	25
Total	45	17	

Site of origin:

Site	Node positive	Node negative	Total
Glans	11	19	26
Prepuce	3	13	12
Coronal sulcus	2	4	6
Shaft	1	-	1

Type of lesion:

Morphology	Node positive	Node negative	Total
Ulcer	11	13	24
Growth	6	15	21

Grade of the tumor:

Grade	Node +ve	Node -ve	Total	%
Well differentiated	3	20	25	12
Moderately differentiated	11	8	17	64.7
Poorly differentiated	3	-	3	100

Poorly differentiated and moderately differentiated tumors had a very strong association with nodal involvement.

COMPARISON STUDY:

1. The study by Fraley et al 1989, Ravi 1993 Hozenblum associates showed that higher grade was associated with increased nodal spread.
2. The study reports by Dean 1935, Maveral et al 1962, and Ornellas et al 1994, all showed that ulcerative growth had earlier nodal metastasis than proliferative type of lesion.
3. John H Beggs & John S.Spratt 1961 showed that shaft involvement was associated with increased incidence on nodes. If the proximal shaft was involved the risk was more.

TREATMENT

In almost all the patients, surgery was the prime modality of treating the primary. Three patients presented with inoperable disease and hence were given radiotherapy.

The type of surgery was either partial or total amputation with perineal urethrostomy and emasculation. Circumcision alone was used as a treatment in any of the 45 cases.

Type of surgery	Number of cases	%
Partial amputation	28	66.7%
Total amputation + urethrostomy	14	33.3%

In almost all the patients who presented with advanced lesions, none of them were suitable candidates for radiotherapy as the primary modality. Radiotherapy was employed only in inoperable cases as far as the treatment of primary is concerned. There had been no mortality so far in the follow up period even in the patients employed radiotherapy. However radiotherapy was widely used in managing the groin.

The regional nodes were either given radiotherapy or ilioinguinal block dissection. Initial 3 patients who presented with inoperable disease and 3 patients who developed inoperable inguinal metastasis after primary surgery were given radiotherapy.

Type of treatment	Number	Percentage
Radiotherapy	6	35.2%
Ilioinguinal block dissection	11	64.7%
Total	17	100%

COMPLICATIONS

The primary lesion was secondarily infected in many of the cases. Meatal stenosis and urethral stricture was observed in 3 cases. All underwent instrumental dilatation.

At the primary site minor wound infection occurred postoperatively.

4 cases developed flap necrosis, 1 case had a sinus tract at the operated site which was excised.

One case developed ulceration at the perineal urethrostomy site.

FOLLOW UP

The cases were followed for a period ranging from 6 months to 2 years. For the primary lesion 2 cm clearance was adequate in all cases of partial amputation and no recurrence was noted

All the recurrences were only at the regional nodes. All the 3 cases which developed fixed nodes on follow up in the clinically node impalpable group of 15 patients came only after a long gap of almost an year and are at present being treated by radiotherapy. On analyzing the cases that recurred, several factors like T stage, grade of the tumor, size of the lesion and morphological type, whether ulcerative or proliferate played a role. Hence these factors should be taken into account while deciding on the treatment modality.

RESULTS

1. The maximum incidence was found to be in the age group 40-50.
2. Carcinoma penis was found to occur in a younger age group compared to western studies.
3. Commonest symptom of presentation was growth (51.1%)
4. The most common site of origin was Glans penis
5. Ulcerative lesion was more common than proliferative type (53.3%)
6. 67% of cases presented with palpable nodes at presentation.
7. 56.7% of the palpable nodes were pathologically positive.
8. 33.3% of cases did not have palpable nodes at presentation.
9. 20% of clinically negative nodes harbored metastasis.
10. Sensitivity of FNAC was about 64.7%.
11. The average time interval between onset of symptoms and seeking medical advice is 9.5 months which is more than western population.
12. Ulcerative lesions had a slightly higher incidence of nodal involvement.
13. Lesions originating from the prepuce had less incidence of nodal involvement when compared to lesions originating from corona and shaft
14. Moderately and poorly differentiated tumors had a very strong association with nodal involvement.
15. Surgery was the primary modality used in the treatment of both primary and secondary.

CONCLUSION

The incidence of palpable nodes at presentation in our study was higher when compared to western studies. However the incidence of pathologically involved nodes is similar. The remaining nodes were inflammatory. This was due to higher rate of secondary infection in our patients due to poor personal hygiene.

Ulcerative lesions, higher stage and grade were more associated with nodal involvement. These factors should be considered while planning the treatment of inguinal nodes.

Only 56.7% of the clinically palpable nodes were actually positive pathologically and 20% of clinically negative nodes eventually developed metastasis.

Carcinoma penis occurred at a lower age compared to western population.

Most of the patients presented in stage III and average delay in seeking advice is around 9 months. Ulcerative type of lesion was more common and commonest site of origin was Glans.

Surgery was the main modality of treatment adopted for the primary and pathologically positive secondaries. However nodal metastasis were found in patients managed conservatively for the clinically negative groin in high grade primary treated by surgery.

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PROFORMA

NAME: PRESENTING SYMPTOMS: PAST HISTORY

AGE: GROWTH/ ULCER: PREMALIGNANT LESION

IP NO: DISCHARGE: MULTIPLE PARTNERS

RELIGION: ING. NODES: STD:

SINGLE/MULTIPLE

OCCUPATION: UNI/BILATERAL

SUPERFICIAL/DEEP

INCOME:

D.O.A DIFFICULTY IN MICTURITION

D.O.D PAIN/WEIGHT LOSS

ADDRESS:

SYSTEMIC EXAMINATION:

CVS: RS:

CNS: ABDOMEN

GENERAL EXAMINATION:

BUILT & NOURISHMENT

PULSE & BP:

LOCAL EXAMINATION:

CIRCUMCISED OR NOT

FLAT/ ULCERATIVE

SITE/SIZE/INFILTRATION

NODES:

AT PRESENTATION

INVESTIGATIONS:

BIOPSY REPORT:

SURGERY:

HISTOPATHOLOGY REPORT:

DIFFERENTIATION:

COMMENTS:

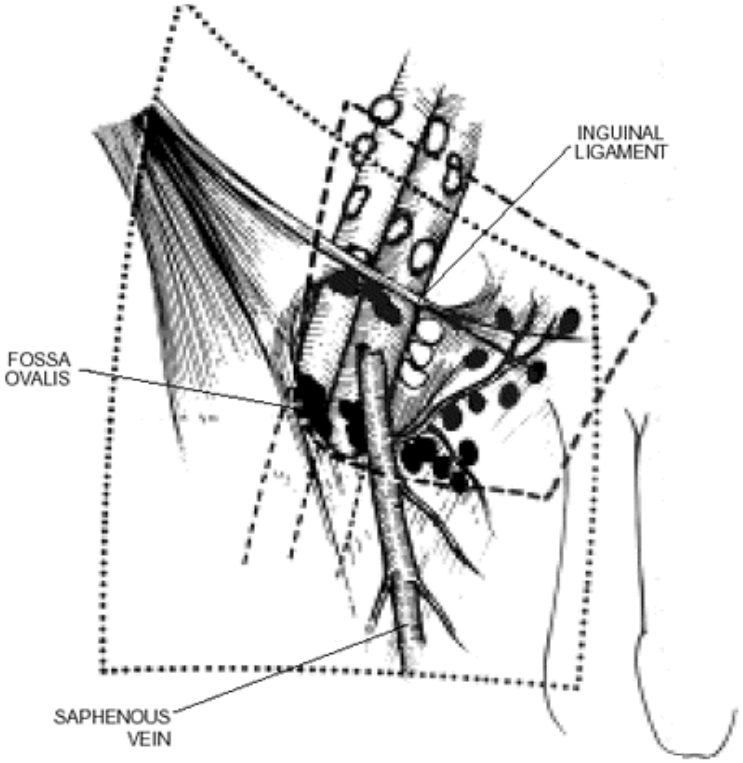
RADIOTHERAPY:

CHEMOTHERAPY:

COMPLICATIONS:

FOLLOW UP:

BOUNDARIES OF ILIO INGUINAL BLOCK DISSECTION



DOTTED LINE:

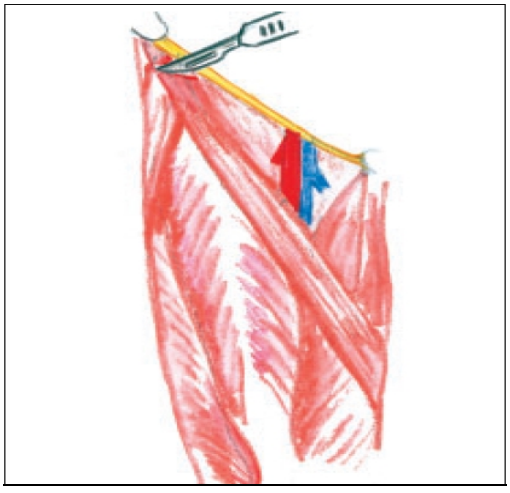
CLASSICAL TYPE

DISCONNECTED LINE:

MODIFIED DISSECTION

(CATALONA)

TRANSPOSITION OF SARTORIUS



GROIN DEFECT AFTER DISSECTION

MASTER CHART

MASTER CHART

S.NO	NAME	AGE	IP NO.	RELIGION	PRESENTING SYMPTOMS	DURATION	H/O CIRCUMCISION	SITE OF ORIGIN	TYPE OF LESION	NODES CLINICAL	NODES PATHOLOGICAL	GRADE	T	N	M	JACKSON	TREATMENT OF PRIMARY	TREATMENT OF GROIN	RECURRENCE	STD	COMPLICATION	TREATMENT OF RECURRENCE
1	GOVINDAN	32	886562	H	U	1yr	-	GL	U	-	-	MD	T1	N0	M0	II	PA	-	-	-	-	-
2	GANAPATHY	41	884456	H	G	1yr	-	P	G	+	-	WD	T1	N1	M0	III	TA	-	-	-	-	-
3	KARTHIKEYAN	54	884333	H	U,N	9m	-	GL	U	+	+	MD	T2	N1	M0	II	TA	IIBD	-	-	FN	-
4	VEDACHALAM	33	887645	H	G	11m	-	GL	G	-	-	WD	T1	N0	M0	I	PA	-	-	-	-	-
5	ARULANANTHAM	44	886532	H	U	9m	-	P	U	-	-	MD	T2	N1	M0	III	TA	-	+	+	-	RT
6	DESAPPAN	55	889675	H	D	8m	-	C	U	+	+	PD	T2	N3	M0	IV	RT	RT	-	-	-	-
7	KARUNANIDHI	38	889343	H	G,Ur	9m	-	GL	G	-	-	WD	T1	N0	M0	II	PA	-	-	-	MS	-
8	RAMAMOORTHY	57	888965	H	U	10m	-	GL	U	+	-	WD	T1	N1	M0	III	PA	-	-	-	-	-
9	PONNUSAMY	43	883434	H	G	8m	-	P	G	+	+	MD	T1	N2	M0	III	TA	IIBD	-	-	-	-
10	MUNIYAN	58	886555	H	U	10 m	-	GL	U	+	-	WD	T1	N1	M0	III	PA	-	-	-	-	-
11	MAHALINGAM	37	879887	H	G	9 m	-	GL	G	-	-	WD	T1	N0	M0	I	PA	-	-	-	-	-
12	KALIYAN	47	891234	H	U,N	10 m	-	GL	U	+	+	MD	T2	N2	M0	III	TA	IIBD	-	-	FN	-
13	RAMAIAH	46	878988	H	G,D	6 m	-	GL	G	+	-	WD	T2	N1	M0	III	PA	-	-	-	-	-
15	GOVINDAN	49	884450	H	U	1yr	-	GL	U	-	-	MD	T1	N0	M0	II	PA	-	-	-	-	-
16	GANAPATHY	50	884233	H	G	1yr	-	P	G	+	-	WD	T1	N1	M0	III	TA	-	-	-	-	-
17	KARTHIKEYAN	51	884015	H	U,N	9m	-	GL	U	+	+	MD	T2	N1	M0	II	TA	IIBD	-	-	FN	-
18	VEDACHALAM	51	883798	H	G	11m	-	GL	G	-	-	WD	T1	N0	M0	I	PA	-	-	-	-	-
19	ARULANANTHAM	52	883581	H	U	9m	-	P	U	-	-	MD	T2	N1	M0	III	TA	-	+	+	-	RT
20	DESAPPAN	53	883364	H	D	8m	-	C	U	+	+	PD	T2	N3	M0	IV	RT	RT	-	-	-	-
21	KARUNANIDHI	53	883147	H	G,Ur	9m	-	GL	G	-	-	WD	T1	N0	M0	II	PA	-	-	-	MS	-
22	RAMAMOORTHY	54	882930	H	U	10m	-	GL	U	+	-	WD	T1	N1	M0	III	PA	-	-	-	-	-
23	PONNUSAMY	55	882713	H	G	8m	-	P	G	+	+	MD	T1	N2	M0	III	TA	IIBD	-	-	-	-
24	MUNIYAN	55	882496	H	U	10 m	-	GL	U	+	-	WD	T1	N1	M0	III	PA	-	-	-	-	-
25	MAHALINGAM	56	882279	H	G	9 m	-	GL	G	-	-	WD	T1	N0	M0	I	PA	-	-	-	-	-
26	RAMU	64	891222	H	U	11m	-	C	U	+	-	MD	T1	N0	M0	II	PA	IIBD	-	-		-

S.NO	NAME	AGE	IP NO.	RELIGION	PRESENTING SYMPTOMS	DURATION	H/O CIRCUMCISION	SITE OF ORIGIN	TYPE OF LESION	NODES CLINICAL	NODES PATHOLOGICAL	GRADE	T	N	M	JACKSON	TREATMENT OF PRIMARY	TREATMENT OF GROIN	RECURRENCE	STD	COMPLICATION	TREATMENT OF RECURRENCE
																					ST	
27	MARIMUTHU	41	885674	H	U	10 m	-	P	U	+	-	WD	T1	N1	M0	III	PA	-	-	-	-	-
28	KALIMUTHU	42	886734	H	G,Ur	6 m	-	C	G	-	-	MD	T2	N1	M0	III	TA	-	-	+	MS	-
29	DASS	55	891256	C	G	7 m	-	GL	G	+	-	WD	T1	N1	M0	III	PA	-	-	-	-	-
30	CHANDRAN	46	891476	H	G,D	7 m	-	GL	G	+	+	WD	T1	N1	M0	III	PA	IIBD	-	-	-	-
31	MUNIYANDI	78	884367	H	G,D,E,C	14 m	-	C	G	-	-	WD	T2	N0	M0	I	TA	-	-	-	-	-
32	DEVAN	47	878956	H	U	9 m	-	GL	U	+	+	MD	T2	N2	M0	III	TA	IIBD	-	-	FN	-
33	PRASANNA	25	892367	H	D,U	7 m	-	P	U	-	-	WD	T1	N0	M0	II	PA	-	-	-	-	-
34	SUBRAMANI	44	884653	H	G	10 m	-	GL	G	+	+	MD	T1	N1	M0	III	PA	IIBD	-	-	-	-
35	ESWARAN	41	886793	H	U	9 m	-	P	U	-	-	WD	T1	N0	M0	I	PA	-	-	-	-	-
36	ARIVALAN	64	887456	C	D,U	11 m	-	P	U	+	+	PD	T2	N3	M0	IV	RT	RT	-	-	-	-
37	CHOCKALINGAM	56	891143	H	G	8 m	-	GL	G	+	-	WD	T1	N1	M0	III	PA	-	-	-	-	-
38	GOPAL	79	878567	H	U,N	10 m	-	GL	U	+	-	MD	T2	N1	M0	III	TA	-	-	-	-	-
39	DORAISAMY	59	887654	H	G	8 m	-	GL	G	+	-	WD	T1	N1	M0	III	PA	-	-	-	-	-
40	CHINNAPA	42	891145	H	U	10 m	-	P	U	-	-	MD	T1	N0	M0	II	PA	-	+	-	-	RT
41	SRINIVASAN	65	891243	H	E,C,G	9 m	-	C	G	+	-	WD	T1	N1	M0	III	PA	-	-	-	-	-
42	PARTHIBAN	51	885673	H	G	8 m	-	GL	G	-	-	WD	T1	N0	M0	I	PA	-	-	-	-	-
43	VENKATESH	47	884593	H	D	15 m	-	GL	U	+	+	MD	T2	N2	M0	III	TA	RT	-	+	-	-
44	VEMBULI	52	894567	H	U	7 m	-	GL	U	+	+	MD	T2	N1	M0	III	TA	IIBD	-	-	-	-
45	VENKAIAH	48	883478	H	D,U	7 m	-	P	U	-	-	WD	T1	N0	M0	II	PA	-	-	-	-	-

(H- Hindu, C- Christian, U- Ulcer, G- Growth, Ur- Urinary symptoms, D- Discharge, E & C- Edema & Cellulitis, N- Node, GL- Glans, P- Prepuce, C- Corona, S- Shaft, WD- Well Differentiated, MD- Moderately Differentiated, PD- Poorly Differentiated, PA- Partial Amputation, TA- Total Amputation, IIBD- Ilio Inguinal Block Dissection, RT- Radio Therapy, MS- Meatal Stenosis, FN- Flap Necrosis, ST- Sinus Tract)